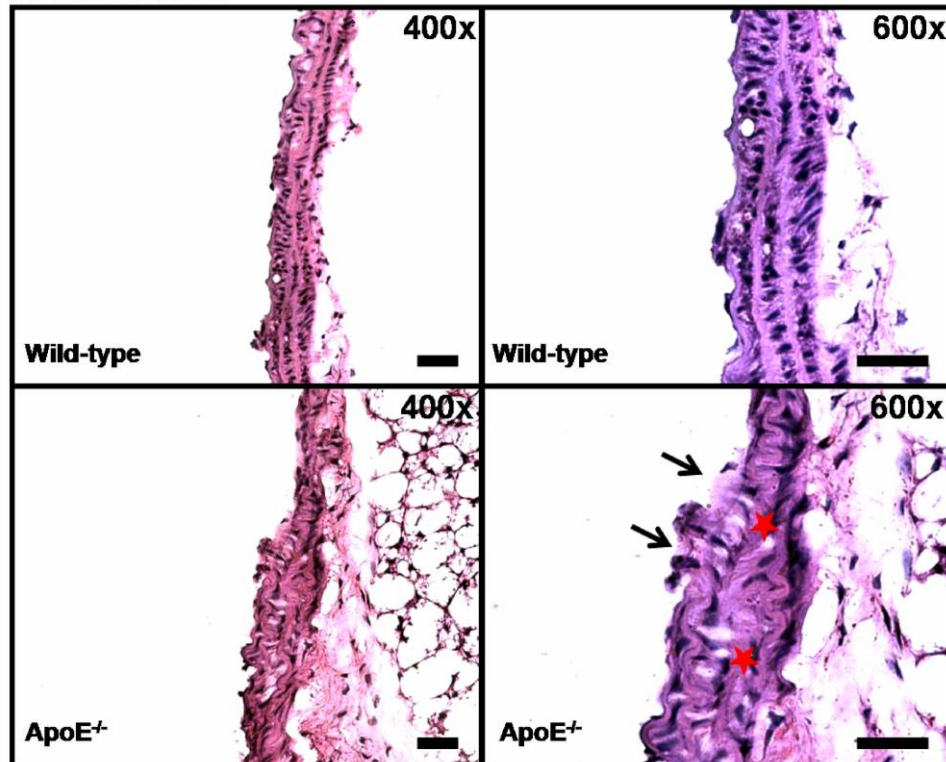


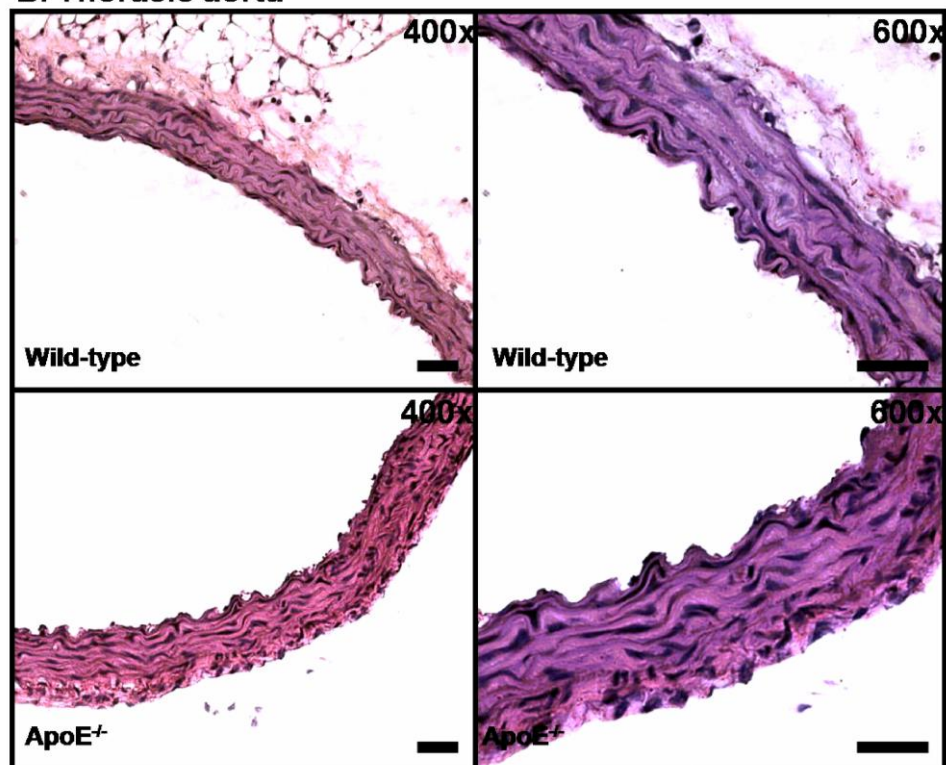
Results

Blood cholesterol, triglycerides and glucose levels in ApoE^{-/-} mice were 383±22.9 mg.dl⁻¹ (p<0.001), 81±11.0 mg.dl⁻¹ and 95±7.6 mg.dl⁻¹, respectively. The values for wild-type mice were respectively, 125±7.6 mg.dl⁻¹, 98±8.2 mg.dl⁻¹ and 104±12.9 mg.dl⁻¹. ApoE^{-/-} mice showed higher levels of atherogenic lipoprotein LDL and IDL and serum LDL oxidized as compared to wild-type mice. Twelve week-old ApoE^{-/-} mice showed an initial fatty streak formation (deposition foam cells; arrows) in the aortic arch, composed of xanthomized cells and sparse inflammatory infiltration. Discrete smooth muscle disorganization (stars) could also be seen. No advanced (necrotic) lesions were seen in those animals (Supplemental Figure 1A). The thoracic aorta showed morphological and histological structures preserved, without atherosclerosis or other related lesions in the intima, media and adventitia layers. Foam cells or ectopic deposition of lipids were absent (Supplemental Figure 1B).

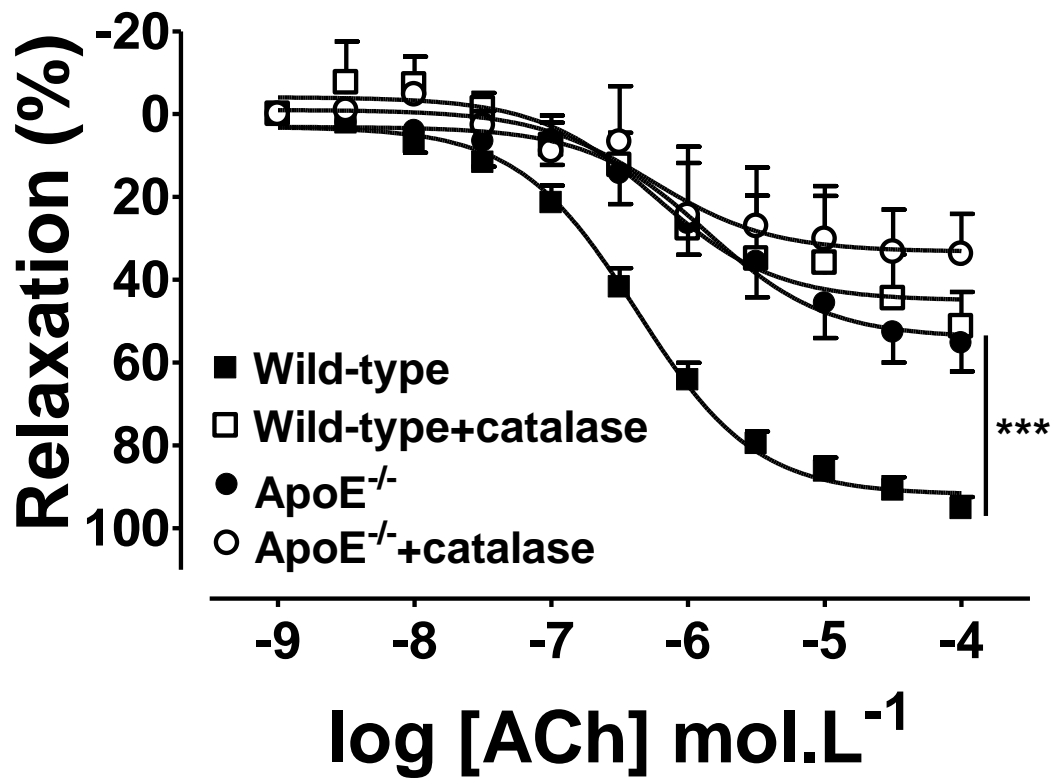
A. Aortic arch



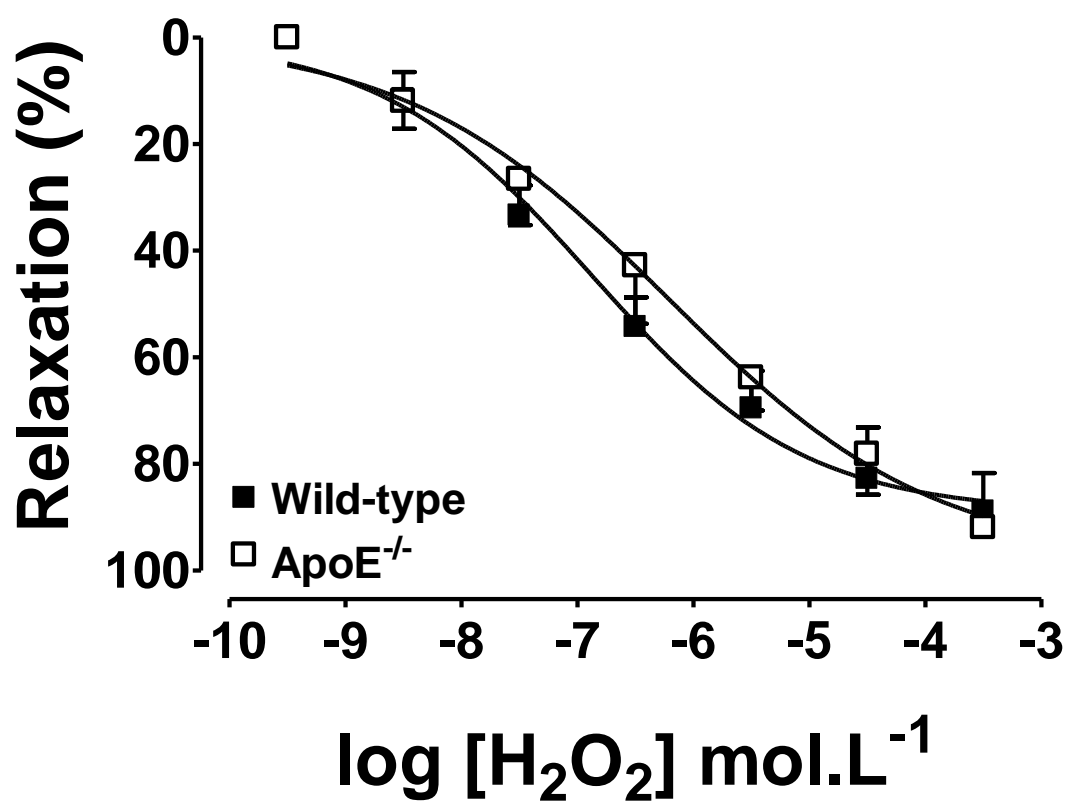
B. Thoracic aorta



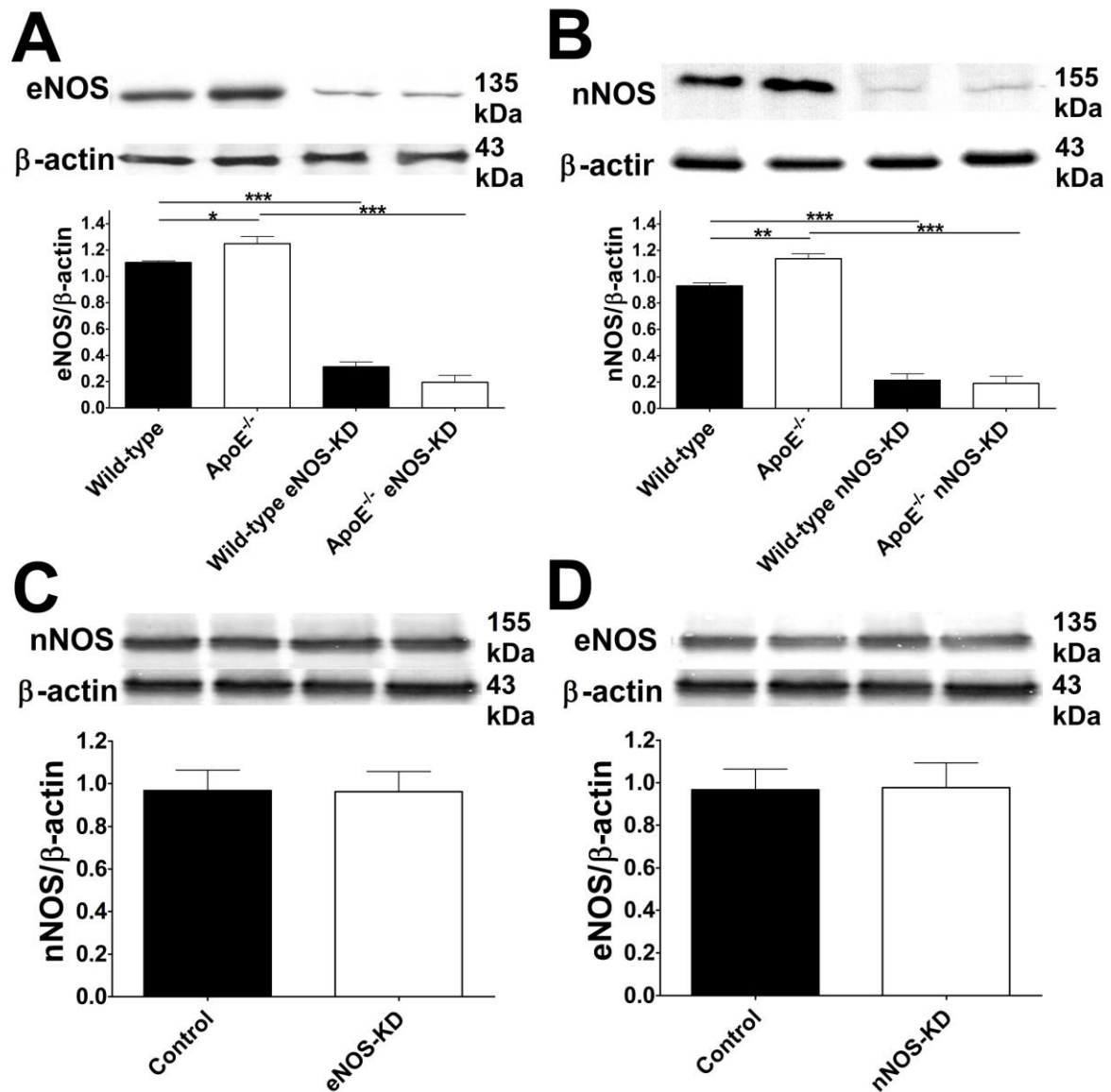
Supplemental Figure I. Morphological analyses in the structure of the aortic arch (A) and thoracic aorta (B) from wild-type and ApoE^{-/-} mice. Representative H&E-stained sections from 5 experiments. Scale bar: 10 μ m.



Supplemental Figure II. Effect of catalase (2400 U.mL⁻¹) on vasodilation induced by acetylcholine (ACh) on wild-type and ApoE^{-/-} mice aortas. The data represent mean \pm SEM of five experiments. ***p<0.001.



Supplemental Figure III. Vasodilator effect of exogenous H_2O_2 in aortas from wild type and $\text{ApoE}^{-/-}$ mice. The experiments were performed in the presence of 50 mmol.L^{-1} aminotriazole (Sigma, St. Louis, MO, USA) to inhibit endogenous peroxidases. The data represent mean \pm SEM of five experiments.



Supplemental Figure IV. Western-blot analysis of the effect of *in vivo* antisense eNOS (eNOS-KD; A) and nNOS (n-NOS-KD; B) knockdown in wild-type and ApoE^{-/-} mice aorta. (C) Control experiments for nNOS in eNOS-KD animals and (D) controls Western-blot for eNOS in nNOS-KD aortas. Images are representative of four experiments. Bar graphs represent mean \pm SEM of four experiments. ***p<0.001.